

REMARKS

Claims 1-79 were pending in the application. Claims 1-29 and 36-79 were withdrawn from consideration as directed to non-elected inventions. Claim 30 has been amended to remove dependency on a withdrawn claim. Claims 32, 33, and 35 have been amended. Claim 34 has been canceled. Claims 80-87 have been added. Support for claims 80-87 can be found throughout the specification and for example at page 10 and 25 of the specification as filed. Upon entry of this amendment claims 30-33, 35 and 80-87 will be pending.

No new matter has been added.

Information Disclosure Statement

The Office alleges that an information disclosure statement (IDS) filed on July 5, 2001 was not accompanied by Form PTO-1449. Applicants enclose a copy of Form PTO-1449 that was filed on July 5, 2001.

Objections

Claims 30-35 stand rejected for allegedly depending on a non-elected claim. Claim 30 has been amended to remove the dependency upon a non-elected claim, thereby rendering the objection moot.

In view of the foregoing, Applicants respectfully request that the objections be withdrawn.

Rejection under 35 U.S.C. § 101

Claims 30-35 stand rejected under 35 U.S.C. § 101 because the claimed invention is allegedly not supported by a specific, substantial and credible asserted utility or a well established utility. The Office also alleges that "the instant application has provided a description of an isolated protein. However, the instant application does not disclose a

specific and substantial biological role of this protein or its significance.” (Office Action, page 3). Applicants respectfully disagrees.

Utility Examination Guidelines

The Utility Examination Guidelines require a claimed invention have a specific, substantial and credible asserted utility, or, alternatively a well-established utility. As Applicants have asserted utilities that are specific, substantial and credible and well-established, thus the Utility Requirement has been satisfied. Applicants therefore respectfully request the withdrawal of the rejection under 35 U.S.C. § 101.

The Utility Examination Guidelines require a claimed invention to have a utility that is specific to the subject matter claimed (a “specific utility”). The present application recites at, for example, pages 33-34 and 37 of the specification that the claimed invention can be used, *inter alia*, to identify ligands and/or protein binding partners. Additionally, the polypeptides of the present invention can be used to generate antibodies useful to localize the protein *in vivo* or *in vitro*. For example, the specification teaches that nGCP-1025 is expressed in the brain and testis. Thus, antibodies generated against the polypeptides of the present invention can be used to identify the origin of cells and/or tissues as being from the brain and/or testis. Furthermore, the antibodies raised against the polypeptides of the present invention can be used to identify specific tissue types, such as the cerebellum and the cerebrum (see, specification, Example 5, pp. 64-65). Being able to identify specific tissue types in the brain can also be used to identify defects and abnormalities in the brain by the absence or presence of staining of nGPCR-1025. It also allows the skilled-artisan to follow the development of the fetal brain to determine when the cerebellum and the cerebrum are developed based upon the antibody staining of nGPCR-1025. Thus, there is no question that Applicants have asserted at least one specific utility and, in fact, have provided numerous specific utilities for the polypeptides of the present invention.

Additionally, the Office appears to be under the assumption that *absolute* certainty is required for a polypeptide to have a specific utility. The Office states, “There

is little doubt that, after complete characterization, this protein will probably be found to have a patentable utility. This further characterization, however, is part of the act of invention and, until it has been undertaken, Applicant's claimed invention is incomplete." (Office Action, page 3).

The standard applicable in this case is not, however, proof to certainty, but rather proof to reasonable probability as the Supreme Court stated applicant need only prove a "substantial likelihood" of utility; certainty is not required. *Brenner v. Manson*, 383 U.S. at 532. Although, there may be numerous inventions that may arise from the present application this standard does not justify the Office's stance that the present invention lacks a specific utility. Thus, Applicants have complied with the specific utility requirement.

The Claimed Invention Has A Substantial Utility

The Utility Examination Guidelines also require a claimed invention to have a utility that defines a real-world use (a "substantial utility"). Applicants teach, as described above, that the claimed invention can be used to make antibodies, identify ligands and other binding partners, such as other proteins that interact with the polypeptide (i.e. a G protein). Thus, it is clear that the claimed invention has real-world uses. All the uses described in the present application are real-world uses and, again, stand in stark contrast to the "throw away" uses (e.g., landfill component or snake food) set forth in the utility guidelines. Thus, there is no question that Applicants have asserted at least one substantial utility and, in fact, have provided numerous substantial utilities. Accordingly, Applicants have complied with the substantial utility requirement.

The Claimed Invention Has A Credible Utility

In addition to a specific and substantial utility the Utility Examination Guidelines require that such utility be credible (a "credible utility"). That is, whether the assertion of utility is believable to a person of ordinary skill in the art based on the totality of evidence and reasoning provided. Clearly, the numerous specific and substantial utilities asserted by Applicants are credible. Assertions of credibility are credible unless "(A) the logic underlying the assertion is seriously flawed, or (B) the facts upon which the

assertion is based is inconsistent with the logic underlying the assertion.” (See, Revised Interim Utility Guidelines Training Materials.) Further, PTO personnel are reminded that they must treat as true a statement of fact made by Applicants in relation to an asserted utility, unless countervailing evidence can be provided that shows that one of ordinary skill in the art would have a legitimate basis to doubt the credibility of such a statement. All the utilities described for the polypeptide are based on sound logic. Furthermore, the utilities for the claimed polypeptides and are *not* inconsistent with the logic underlying the assertion that the polypeptides are useful. Polypeptides are useful to generate antibodies, identify ligands or protein partners, evaluate expression patterns, evaluate protein activity, etc. The Office provides no evidence that the logic is seriously flawed or that the facts upon which these assertions are based is inconsistent with the logic underlying the assertions.

The Examiner cites literature allegedly identifying difficulties that may be involved in predicting protein function. None of the cited references, however, suggests that functional homology cannot be inferred by a reasonable probability in any particular case. It is well-known that the probability that two unrelated polypeptides share more than 40% sequence homology over 70 amino acid residues is exceedingly small. Brenner et al., *Proc. Natl. Acad. Sci.* **95**:6073-78 (1998) (See, Attached reference). In the present application homology is in excess of 40% over many more than 70 amino acid residues. The probability, therefore, that the polypeptide encoded for by the claimed polynucleotides is related to the reference polypeptides is, accordingly, very high. None of the references cited by the Examiner contradicts Brenner's basic rule. At most, references cited by the USPTO individually and together stand for the proposition that it may be difficult to make predictions about function with certainty, however this is not the “countervailing evidence” required by the Utility Examination Guidelines. Therefore, no countervailing evidence that says the present invention does not have a substantial, credible, and useful invention has been provided.

Furthermore, GPCR proteins have a well established utility. Many medically significant biological processes are mediated by signal transduction pathways involving

G-proteins and other second messengers, and G protein coupled seven transmembrane receptor proteins are recognized as important therapeutic targets for a wide range of diseases. According to a recently issued United States patent, nearly 350 therapeutic agents targeting GPCRs have been successfully introduced onto the market in only the last fifteen years. (See U.S. Patent No. 6,114,127, at col. 2, lines 45-50.) A recent journal review reported that most GPCR ligands are small and can be mimicked or blocked with synthetic analogues. That, together with the knowledge that numerous GPCRs are targets of important drugs in use today, make identification of GPCRs "a task of prime importance." (See, Marchese et al., Trends Pharmacol. Sci., 20(9): 370-5., 1999, Attached hereto) Thus, the allegations that there is no well established utility for proteins of the class that the Applicants are now claiming is directly refuted by industry evidence.

In this respect, the G protein coupled receptor family is analogous to the chemical genus that was the subject of *In re Folkers*, 145 USPQ 390 (CCPA 1965) (Compound that belongs to class of compounds, members of which are recognized as useful, is considered useful under §101.) The Patent Office does not serve the public by attempting to substitute a formulaic analysis of § 101 for the established judgment of the biopharmaceutical industry as to what is "useful." If the Patent Office is aware of any well-grounded scientific literature suggesting that GPCR's are not useful, the Applicants request that it be made of record.

Art-Recognized Utility

The Utility requirement may also be satisfied by an "Art Established Utility" which means that "a person of ordinary skill in the art would immediately appreciate why the invention is useful based on the characteristics of the invention... and the utility is specific, substantial and credible." (M.P.E.P. §2107).

Applicants note for the record that the patent office apparently agrees with Applicant's reasoning that GPCRs are useful in that the Office has granted and apparently continues to grant patents to G-protein coupled receptors, their encoding polynucleotides and antibodies directed to them *in which no natural substrate or*

specific biological significance is ascribed to the protein. Specifically, Applicants would like to bring the following US Patents to the Office's attention:

6,518,414 MacLennan "Molecular Cloning and Expression of G-Protein Coupled Receptors" (Claims an isolated polynucleotide)

6,511,826 Li et al. "Polynucleotides Encoding Human G-Protein Chemokine Receptor (CCR5) HDG NR10" (Claims an isolated polynucleotide encoding a protein identified as a "chemokine receptor" with no specific chemokine identified)

6,372,891 Soppet et al. "Human G-Protein Receptor HPRAJ70" (Claims an antibody directed to a G-protein coupled receptor)

6,361,967 Agarwal et al. "AXOR10, A G-Protein Coupled Receptor" (Claims an isolated polynucleotide)

6,348,574 Godiska et al. "Seven Transmembrane Receptors" (Claims an antibody directed to a G-protein coupled receptor)

6,114,139 Hinuma et al. "G-Protein Coupled Receptor Protein and A DNA Encoding the Receptor" (Claims an isolated polynucleotide).

6,111,076 Fukusumi et al. "Human G-Protein Coupled Receptor (HIBCD07)" (Claims isolated polypeptide)

6,107,475 Godiska et al. "Seven Transmembrane Receptors" (Claims isolated polynucleotide and methods)

6,096,868 Halsey et al. "ECR 673: A 7-Transmembrane G-Protein Coupled Receptor" (Claims isolated polypeptide)

6,090,575 Li et al. "Polynucleotides Encoding Human G-Protein Coupled Receptor GPR1" (Claims isolated polynucleotide)

6,071,722 Elshourbagy et al. "Nucleic Acids Encoding A G-Protein Coupled 7TM Receptor (AXOR-1)" (Claims an isolated polynucleotide)

6,071,719 Halsey et al. "DNA Encoding ECR 673: A 7-Transmembrane G-Protein Coupled Receptor" (Claims an isolated polynucleotide)

6,060,272 Li et al. "Human G-Protein Coupled Receptors" (Claims isolated polynucleotide)

6,048,711 Hinuma et al. "Human G-Protein Coupled Receptor Polynucleotides" (Claims isolated polynucleotide)

6,030,804 Soppet et al. "Polynucleotides Encoding G-Protein Parathyroid Hormone Receptor HLT DG74 Polypeptides" (Claims isolated polynucleotide)

6,025,154 Li et al. "Polynucleotides Encoding Human G-Protein Chemokine Receptor HDG NR10" (Claims an isolated polynucleotide encoding a protein identified as a "chemokine receptor" with no specific chemokine identified)

5,998,164 Li et al. "Polynucleotides Encoding Human G-Protein Coupled Receptor GPRZ" (Claims isolated polynucleotide)

5,994,097 Lal et al. "Polynucleotide Encoding Human G-Protein Coupled Receptor" (Claims isolated polynucleotide)

5,958,729 Soppet et al. "Human G-Protein Receptor HCEGH45" (Claims isolated polypeptide)

5,955,309 Ellis et al. "Polynucleotide Encoding G-Protein Coupled Receptor (H7TBA62)" (Claims isolated polynucleotide)

5,948,890 Soppet et al. "Human G-Protein Receptor HPRAJ70" (Claims isolated polypeptide)

5,945,307 Glucksmann et al. "Isolated Nucleic Acid Molecules Encoding A G-Protein Coupled Receptor Showing Homology to The 5HT Family of Receptors" (Claims isolated polynucleotide)

5,942,414 Li et al. Polynucleotides Encoding Human G-Protein Coupled Receptor HIBEF51" (Claims isolated polynucleotide)

5,912,335 Bergsma et al. "G-Protein Coupled Receptor HUVCT36" (Claims isolated polynucleotide)

5,874,245 Fukusumi et al. "Human G-Protein Coupled Receptors (HIBCD07)" (Claims isolated polynucleotide)

5,871,967 Shabon et al. "Cloning of A Novel G-Protein Coupled 7TM Receptor" (Claims isolated polynucleotide)

5,869,632 Soppet et al. "Human G-Protein Receptor HCEGH45" (Claims isolated polynucleotide)

5,856,443 MacLennan et al. "Molecular Cloning and Expression of G-Protein Coupled Receptors" (Claims isolated polynucleotide)

5,834,587 Chan et al. "G-Protein Coupled Receptor, HLTEX11" (Claims isolated polypeptide)

5,776,729 Soppet et al. "Human G-Protein Receptor HGBER32" (Claims isolated polynucleotide)

5,763,218 Fujii et al. "Nucleic Acid Encoding Novel Human G-Protein Coupled Receptors" (Claims isolated polynucleotide)

5,756,309 Soppet et al. "Nucleic Acid Encoding A Human G-Protein Receptor HPRAJ70 and Method of Producing the Receptor" (Claims isolated polynucleotide)

5,585,476 MacLennan "Molecular Cloning and Expression of G-Protein Coupled Receptors" (Claims isolated polynucleotide)

5,759,804 Godiska et al. "Isolated Nucleic Acid Encoding Seven Transmembrane Receptors" (Claims isolated polynucleotide and methods)

Applicants submit that these issued US Patents are evidence of an art recognized utility for G-protein coupled receptors whose natural ligand is unknown. If the Patent Office's position is that issued patents are *not* sufficient evidence of art recognition then Applicants respectfully request that this position be made of record. In the alternative, if the Patent Office wishes to take the position that these issued patents are directed to non-statutory subject matter, then Applicants respectfully request that this position be made of record as well.

In view of the foregoing, Applicants respectfully requests that the rejection under 35 U.S.C. § 101 be withdrawn.

Rejections under 35 U.S.C. § 112

Claims 30-35 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to adequately teach how to use the instant invention. According to the Office, “Since the claimed invention is not supported by a specific, substantial, and credible asserted utility or a well established utility...one skilled in the art clearly would not know how to use the claimed invention.” (Office Action, page 5) Applicants respectfully disagree.

As discussed above, the present invention *is* supported by a specific, substantial, and credible asserted utility as well as a well established utility. Accordingly, Applicants respectfully request that the rejection be withdrawn.

The Office also alleges, that “even if the claims possessed utility... claim 33 would still be rejected under 35 U.S.C. § 112, first paragraph, because the specification, while then enabling for the polypeptide of SEQ ID NO:2, does not reasonably provide enablement for a polypeptide of SEQ ID NO:2 having at least one conservative amino acid substitution.” (Office Action, page 5). Applicants respectfully disagree.

As presently amended, claim 33, recites, “The polypeptide of claim 32 wherein said amino acid sequence is at least 80% homologous to SEQ ID NO:2.” The claim, as amended, is not excessively broad. A person of ordinary skill in the art would understand what is meant by “at least 80% homologous.” Homology for a polypeptide is well understood by those of ordinary skill in the art and is described in the specification such that the present invention can be made and used by the art-skilled (see for example, specification, pp. 23, - p. 24). Thus, claim 33 is completely enabled.

In view of the foregoing, Applicants respectfully request that the rejection of claim 33 under 35 U.S.C. § 112, first paragraph be withdrawn.

Claims 34 and 35 stand rejected under 35 U.S.C. § 112, first and second paragraphs because allegedly “the claimed invention is not described in such full, clear, concise and exact terms as to enable any person skilled in the art to make and use the same, and/or for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.” (Office Action, page 6). Applicants respectfully disagree.

The Office alleges that the term “allelic variant” does not “have any particular connotation as to the encoded protein.” Although Applicants disagrees with the Office’s allegation that “allelic variant” is indefinite and/or not enabled, in order to further prosecution, Applicants have canceled claim 34 and amended claim 35 so that it now depends on claim 30 instead of claim 34.

Accordingly, Applicants respectfully requests the rejection of claims 34 and 35 under 35 U.S.C. § 112, first and second paragraphs be withdrawn.

Conclusion

Applicants believe the claims are in condition for allowance. An early Notice of Allowance is therefore earnestly solicited. Applicants invite the Examiner to contact the undersigned at (215) 665-6914 to clarify any unresolved issues raised by this response.

Attached hereto is a copy of Form PTO-1449 filed on July 5, 2001 and copies of Brenner *et al.* and Marchese *et al.*

Respectfully submitted,



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